

- 33 -

## CLAIMS

1. A method of inhibiting a proinflammatory immune response in a mammal comprising administering an effective amount of a ligating agent which causes ligation of Fc $\gamma$ RI receptors on cells of the mammal.

2. A method according to claim 1 wherein the ligating agent comprises a multivalent antibody which binds to the Fc $\gamma$ RI receptor.

3. A method according to claim 1 wherein the ligating agent comprises an immune complex containing at least two antibody molecules or fragments thereof which contain the Fc region of IgG.

4. A method according to claim 1 wherein the ligating agent comprises an antibody multimer containing at least two antibody molecules or fragments thereof which contain the Fc region of IgG.

5. A method according to claim 4 wherein the ligating agent comprises an IgG preparation comprising IgG dimers, IgG trimers, or a combination thereof.

6. A method according to claim 5 wherein the IgG content of the IgG preparation comprises, on a weight percent basis, at least about 50% IgG dimers, IgG trimers, or a mixture thereof.

7. A method according to claim 1 wherein the ligating agent does not cause ligation of Fc $\gamma$ RIII receptors.

8. A method of inhibiting a proinflammatory immune response in a mammal comprising administering an IgG antibody which binds to antigen in the mammal to form an immune complex capable of ligating Fc $\gamma$ RI receptors present on host cells.

- 34 -

9. A method according to claim 8 wherein the immune complex does not cause ligation of Fc $\gamma$ RIII receptors.

10. A method for treating or preventing shock associated with bacterial endotoxemia comprising administering to a mammal in need of such treatment an effective amount of ligating agent which causes ligation of Fc $\gamma$ RI receptors on cells of the mammal.

11. A method according to claim 10 wherein the ligating agent comprises an immune complex containing at least two antibody molecules or fragments thereof which contain the Fc region of IgG.

12. A method according to claim 10 wherein the ligating agent comprises a multivalent antibody which binds to the Fc $\gamma$ RI receptor.

13. A method according to claim 10 wherein the ligating agent comprises an antibody multimer containing at least two antibody molecules or fragments thereof which contain the Fc region of IgG.

14. A method according to claim 13 wherein the ligating agent comprises an IgG preparation comprising IgG dimers, IgG trimers, or a combination thereof.

15. A method according to claim 14 wherein the IgG content of the IgG preparation comprises, on a weight percent basis, at least about 50% IgG dimers, IgG trimers, or a mixture thereof.

16. A method according to claim 10 wherein the ligating agents does not cause ligation of Fc $\gamma$ RIII receptors.

- 35 -

17. A method of treating or preventing shock associated with bacterial endotoxemia in a mammalian host comprising administering an IgG antibody which binds to antigen in the host to form an immune complex capable of ligating FcγRI receptors present on host cells.

18. A method for treating an autoimmune disorder comprising administering to an individual in need of such treatment an effective amount of a ligating agent which causes ligation of FcγRI receptors on cells of the individual.

19. A method according to claim 18 wherein the ligating agent comprises a multivalent antibody which binds to the FcγRI receptor.

20. A method according to claim 18 wherein the ligating agent comprises an immune complex containing at least two antibody molecules or fragments thereof which contain the Fc region of IgG.

21. A method according to claim 18 wherein the ligating agent comprises an antibody multimer containing at least two antibody molecules or fragments thereof which contain the Fc region of IgG.

22. A method according to claim 21 wherein the ligating agent comprises an IgG preparation comprising IgG dimers, IgG trimers, or a combination thereof.

23. A method according to claim 22 wherein the IgG content of the IgG preparation comprises, on a weight percent basis, at least about 50% IgG dimers, IgG trimers, or a mixture thereof.

24. A method according to claim 18 wherein the ligating agent does not cause ligation of FcγRIII receptors.

- 36 -

25. A method according to claim 18 wherein the autoimmune disease is selected from the group consisting of Kawasaki Disease, systemic lupus erythematosus, rheumatoid arthritis, inflammatory bowel disease, Sydenham's chorea, and autoimmune hemolytic anemia.

26. A method according to claim 25, wherein the autoimmune disease is systemic lupus erythematosus.

27. A method for treating an autoimmune disorder in a mammalian host comprising administering an IgG antibody which binds to antigen in the host to form an immune complex capable of ligating FcγRI receptors present on host cells.

28. The method of claim 1, wherein the at least two IgG Fc regions are joined by a covalent bond.

29. The method of claim 1, wherein the at least two IgG Fc regions are joined by a homobifunctional or heterobifunctional cross-linking reagent.

30. The method of claim 29, wherein the homobifunctional cross-linking agent is selected from the group consisting of disuccinimidyl tartrate; disuccinimidyl suberate; ethylene glycolbis(succinimidyl succinate); 1,5-difluoro-2,4-dinitrobenzene; 4,4'-diisothiocyano-2,2'-disulfonic acid stilbene; and bismaleimido-hexane.

- 37 -

31. The method of claim 29, wherein the heterobifunctional cross-linking agent is selected from the group consisting of N-succinimidyl-3-(2-pyridyldithio) propionate; sulfosuccinimidyl-2-(p-azidosalicylamido)ethyl-1-3'-dithiopropionate; N-maleimidobenzoyl-N-hydroxy-succinimidyl ester; m-maleimidobenzoylsulfosuccinimide ester; N-succinimidyl(4-iodoacetyl) aminobenzoate; succinimidyl 4-(N-maleimidomethyl)-cyclohexane-1-carboxylate; succinimidyl-4-(p-maleimidophenyl) butyrate; sulfosuccinimidyl(4-iodoacetyl) aminobenzoate; sulfosuccinimidyl 4-(N-maleimidomethyl) cyclohexane-1-carboxylate; sulfosuccinimidyl 4-(p-maleimidophenyl)-butyrate; bromoacetyl-p-aminobenzoyl-N-hydroxy-succinimidyl ester; and iodoacetyl-N-hydroxysuccinimidyl ester.

32. The method of claim 1, wherein the ligating agent comprises a synthetic or recombinant peptide.

33. The method of claim 10, wherein the at least two IgG Fc regions are joined by a covalent bond.

34. The method of claim 10, wherein the at least two IgG Fc regions are joined by a homobifunctional or heterobifunctional cross-linking reagent.

35. The method of claim 34, wherein the homobifunctional cross-linking agent is selected from the group consisting of disuccinimidyl tartrate; disuccinimidyl suberate; ethylene glycolbis(succinimidyl succinate); 1,5-difluoro-2,4-dinitrobenzene; 4,4'-diisothiocyano-2,2'-disulfonic acid stilbene; and bismaleimidohehexane.

- 38 -

36. The method of claim 34, wherein the heterobifunctional cross-linking agent is selected from the group consisting of N-succinimidyl-3-(2-pyridyldithio)propionate; sulfosuccinimidyl-2-(p-azidosalicylamido)ethyl-1-3'-dithiopropionate; N-maleimidobenzoyl-N-hydroxy-succinimidyl ester; m-maleimido-benzoylsulfosuccinimide ester; N-succinimidyl(4-iodoacetyl) aminobenzoate; succinimidyl 4-(N-maleimidomethyl)-cyclohexane-1-carboxylate; succinimidyl-4-(p-maleimidophenyl)butyrate; sulfosuccinimidyl(4-iodoacetyl)aminobenzoate; sulfosuccinimidyl 4-(N-maleimidomethyl) cyclohexane-1-carboxylate; sulfosuccinimidyl 4-(p-maleimidophenyl)-butyrate; bromoacetyl-p-aminobenzoyl-N-hydroxy-succinimidyl ester; and iodoacetyl-N-hydroxysuccinimidyl ester.

37. The method of claim 10, wherein the ligating agent comprises a synthetic or recombinant peptide.

38. The method of claim 18, wherein the at least two IgG Fc regions are joined by a covalent bond.

39. The method of claim 18, wherein the at least two IgG Fc regions are joined by a homobifunctional or heterobifunctional cross-linking reagent.

40. The method of claim 39, wherein the homobifunctional cross-linking agent is selected from the group consisting of disuccinimidyl tartrate; disuccinimidyl suberate; ethylene glycolbis(succinimidyl succinate); 1,5-difluoro-2,4-dinitrobenzene; 4,4'-diisothiocyano-2,2'-disulfonic acid stilbene; and bismaleimido-hexane.

- 39 -

41. The method of claim 39, wherein the heterobifunctional cross-linking agent is selected from the group consisting of N-succinimidyl-3-(2-pyridyldithio) propionate; sulfosuccinimidyl-2-(p-azidosalicylamido)ethyl-1-3'-dithiopropionate; N-maleimidobenzoyl-N-hydroxy-succinimidyl ester; m-maleimidobenzoylsulfosuccinimide ester; N-succinimidyl(4-iodoacetyl) aminobenzoate; succinimidyl 4-(N-maleimidomethyl)-cyclohexane-1-carboxylate; succinimidyl-4-(p-maleimidophenyl)butyrate; sulfosuccinimidyl(4-iodoacetyl)aminobenzoate; sulfosuccinimidyl 4-(N-maleimidomethyl) cyclohexane-1-carboxylate; sulfosuccinimidyl 4-(p-maleimidophenyl)-butyrate; bromoacetyl-p-aminobenzoyl-N-hydroxy-succinimidyl ester; and iodoacetyl-N-hydroxysuccinimidyl ester.

42. The method of claim 18, wherein the ligating agent comprises a synthetic or recombinant peptide.